PATHOLOGY OF EXPERIMENTAL ACUTE SALMONELLOSIS IN SPECIFIC PATHOGEN FREE SWINE

by

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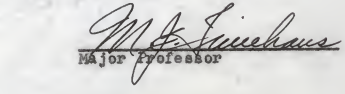

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INTRODUCTION

Salmonellosis causes a considerable economic loss to the swine industry. This loss is hard to determine in dollar value since salmonellosis is often a secondary invader or becomes chronic and causes a poor weight gain, as well as acute death. The symptoms and lesions observed in field cases of salmonellosis are often confused with other swine viral, bacterial, and nutritional conditions which make the diagnosis of this condition difficult. Since Salmonella has been isolated along with other pathogens from diseased swine, this study was undertaken to determine the pathology of a pure infection of Salmonella choleraesuis var. kunzendorf when other pathogens were absent or reduced.

The pigs used in this study were reared in a clean environment in a commercial specific pathogen free (SPF) laboratory and maintained in thoroughly cleaned quarters for the duration of the study. It was believed that the chance for contact and establishment of normal bacterial and viral flora and of some of the widely desiminated swine diseases was greatly lessened so that the primary effect of a Salmonella infection could be more accurately determined.

REVIEW OF THE LITERATURE

Salmonella was first described as an infectious agent in swine in 1885 when Salmon and Smith[24] described an organism, Salmonella choleraesuis (Bacterium of Swine Plague) as the etiological agent in "hog cholera." Later it was suggested by de Schweinitz and Dorset[8] and proven by Dorset et al.[9] in 1905 that

Salmonella was not responsible for "hog cholera" but the condition was due to a filterable virus.

S. choleraesuis was later incriminated as the causitive agent of an enteritis syndrome in swine by Murray et al.[21] in 1927. These workers were able to reproduce the disease and studied the pathology involved both grossly and microscopically and reported their findings in 1928 (Biester et al.[3]). In 1929 Murray et al.[22] reported on the association of S. choleraesuis and Spherophorus necrophorus in enteritis in swine and discussed the bacteriology and immunology associated with this condition. Salmonellosis in swine has been observed in all parts of the world and has been reproduced many times. Shanks and Lamont[29] reproduced salmonellosis from cultures obtained from infected pigs in northern Ireland. Salvin[30] was able to reproduce "necrotic enteritis" by spraying a hog pasture with a culture of S. choleraesuis and also by placing healthy pigs in quarters just vacated by recovered pigs. Schofield[28] was able to experimentally produce salmonellosis in swine by injecting them with S. choleraesuis var. kunzendorf intravenously and by contact with infected pigs. Levine et al.[19] used various species of Salmonella that were recovered from swine on post mortem examination and, although few pigs were used, suggested that "necrotic enteritis" was caused by S. choleraesuis var. kunzendorf. Josland[17] was able to produce salmonellosis in swine while he studied the value of an autogenous bacterin. Kerkamp and Lindorfer[18] produced acute and chronic salmonellosis by feeding a broth culture of S. choleraesuis var. kunzendorf. Guthrie[12] also produced salmonellosis by feeding pigs a culture of S. choleraesuis var. kunzen-

dorf while studying nitrofurazone as a therapeutic agent. Other investigators have not been as successful in the reproduction of the disease. Hindmarch et al.[16] were unable to produce a fatal case of salmonellosis while studying the serological relationship between swine infected with S. choleraesuis var. kunzendorf and serum samples from swine with swine dysentery. They concluded that swine dysentery was not caused by S. choleraesuis var. kunzendorf. Gwatkin and Maynihan[13,14] in a two-part study on Salmonella infections in swine used a total of 14 strains of S. choleraesuis on 102 pigs producing death in two pigs and a transitory infection in many of the others. These authors suggested that S. choleraesuis was not the etiological agent of "necrotic enteritis."

Much other work has been performed on salmonellosis in swine. Salvin[32] was able to determine the infective dose of S. choleraesuis by infecting swine with various numbers of organisms. Dr. Slavin gave from 200,000 to 400,000,000 S. choleraesuis organisms per os. The pigs were observed for eight weeks and the effect was determined by weight gain as compared to controls. He demonstrated that a small number of organisms had a definite effect on these pigs. McBryde[20] described pneumonias in swine resulting from S. choleraesuis infection in garbage fed hogs from California.

Biester[2] described the clinical symptoms of salmonellosis in swine as being; an elevated temperature up to 107 F., rough staring hair, unthriftiness, and sometimes extreme emaciation. A severe profuse diarrhea was generally the case and the age most affected was from three to six months. Hagen and Bruner[15] considered salmonellosis to be associated with hog cholera in older swine

with an occasional outbreak of Salmonella infection occurring in suckling pigs.

Necropsy lesions described by Biester[2] were usually congestion and focal necrosis of the mucosal lining of the fundic portion of the stomach and of the intestine, becoming progressively more severe in the posterior portions of the tract. Microscopically the lesions in the ileum ranged in severity from advance acute catarrhal ileitis to a more severe condition characterized by diffuse cellular infiltration and by many distended crypts which bulged as a result of accumulations of exudate and caseated debris. Some of the solitary lymph nodules in this area had leukocytic infiltration and caseation necrosis. The mucosa of the large intestine was usually covered by a diphtheritic necrotic membrane beneath which was a denuded granular area. Microscopically the mucosa of the large intestine and cecum had undergone almost complete necrosis.

Glasser et al.[11] also described a hyperplasia of the spleen but with no conspicuous softening. The cut surface was a reddish-blue color and the follicles were distinct. Van Es[34] also described a similar condition in the spleen. Glasser et al.[11] described hemorrhages occurring in the kidney cortex under the epicardium and under or on the pleura. In the liver and often in the spleen and kidney were found miliary necrotic areas in the form of reddish or gray foci. Cohrs[6] described a stimulation of the Kupffer cells and endothelial cells of the portal sinusoids in the liver thereby producing a granuloma which was located intralobularly. The granuloma usually contained many macrophages but sel-

dom any other signs of inflammation.

There is a definite interest in S. choleraesuis in the field of public health. S. choleraesuis has been incriminated in several food borne enterotoxemias in humans with at least one report of a fatal case of septicemia developing in a woman in England (Bailey et al.[1]). In survey studies on the incidence of S. choleraesuis, Saphra and Wasserman[25] traced 329 cultures of S. choleraesuis from man and described most infections as chronic carrier states with the source of infection primarily swine. Rubin et al.[23] ran a survey on the incidence of Salmonella in the mesenteric lymph nodes of normal swine presented for slaughter and were able to culture Salmonella sp. from 10% of the hogs studied, with S. typhimurium and S. choleraesuis being the most prevelent strains. In a survey of swine feed stuffs, Smith[33] isolated 12 strains of Salmonella from bone meal and fish meal which were fed to hogs. No pathology developed in these pigs and only one carried the organism at slaughter. These authors emphasized the importance of this chain of events as a possible human source of salmonellosis.

MATERIALS AND METHODS

The culture of Salmonella used in this experiment was obtained from a pig presented for necropsy at Kansas State University. The culture was lyophilized after a pure culture was obtained and stored in this state until the beginning of this project. The virulence of Salmonella was maintained by lyophilization in work done by Schoening et al.[27] At the commencement of this project the culture was removed from the lyophilized state by placing it

in Tryptocase Soy* broth and incubated at 37 C. Subcultures were made to check for purity and for a sample to be typed. The organism was typed by the Kansas State Board of Health laboratory** as Salmonella choleraesuis var. kunzendorf. The kunzendorf variety is most often incriminated in cases of salmonellosis in swine and the most prevelent in the United States (Bruner and Edwards[5]). The culture was passed through mice and through one hog to test its virulence before administration to the experimental pigs. The organism was administrated as a 6-14 hour culture in nutrient broth per os either on the feed or by drenching. The total dosage per pig varied in the different groups of pigs. The organism was checked for purity before administration to each group and on re-isolation by culturing on Brilliant Green Neutral Red Agar§ and sheep blood agar. Brilliant Green Neutral Red Agar has been described as being superior to other differential media for the isolation of S. choleraesuis from contaminated material by Slavin[31]. Gitter[10] also had very good results by using this medium. Biochemical activity was checked by inoculation into Kligler's Iron Agar*, lactose broth, dextrose broth, sucrose broth, mannitol broth, maltose broth, xylose broth, salicin broth, and arabinose broth. The culture used produced acid and gas from dextrose, xylose, maltose, and mannitol. Biochemical changes were negative when grown in lactose, sucrose, arabinose, and salicin[4]. Hydrogen sulfide was produced in Kligler's Iron Agar with the butt of the slant

*Difco Laboratories, inc., Detroit 1, Michigan.
**National Reserve Bldg., Topeka, Kansas.
§Bacto SS Agar, Difco Laboratories, inc., Detroit 1, Michigan.

turning acid and the surface of the slant remaining alkaline. The fact that the culture produced hydrogen sulfide and failed to ferment arabinose was a valuable aid in the identification of S. choleraesuis var. kunzendorf (Bruner and Edwards[5]). The carbohydrate broths used were prepared in Bacto Purple Broth Base* with one per cent of the desired sugar added.

In an attempt to determine the pathogenicity of the organism under study, several commercial pigs were purchased locally. The pigs in pilot study groups one and two were approximately three months of age and the pigs in pilot study groups three, four, five, and six were approximately three weeks of age at the time of purchase.

Pilot study group number one contained two 60-pound pigs which were each given 50 ml. of a 24-hour broth culture of S. choleraesuis var. kunzendorf. The temperature of the pigs was taken twice a day until recovery was evident.

In pilot study group two there were two 75-pound pigs which were each given 50 ml. of a six-hour broth culture that had been passed three times through mice. The culture produced death in the mice in 18 hours following intraperitoneal inoculation. The rectal temperature of these pigs was recorded twice a day until acute symptoms diminished.

The two 25-pound pigs in pilot study group number three were given 50 ml. of a six-hour culture from a freshly reconstituted lyophilized source. The original culture had been lyophilized in several different vials and in this case a new one was opened,

*Difco Laboratories, Inc., Detroit 1, Michigan.

placed in broth, checked for purity, passed into one mouse, and then prepared for the introduction into the pigs. Temperatures were again recorded until recovery was evident.

In pilot study group number four the same culture was used, only this time it was administered to two 30-pound pigs every day for four days in 50 ml. doses. Seven days after the first administration one pig was euthanatized by an intracardial injection of sodium pentabarbital and a necropsy was performed. Attempts to isolate the organism from the tissues were futile.

In pilot study group number five one pig was injected with modified live lapinized hog cholera vaccine* without antiserum. One hundred ml. of the same culture as used in experiment three and four was administered on the second, third, fourth, and fifth days post vaccination. This pig died on the eighth day post vaccination and was necropsied. Salmonella was recovered from the liver, spleen, kidney, and mesenteric lymph nodes. After the biochemical studies were completed it was determined that the recovered strain was the same as the infective strain so this culture was used as the infective culture for the specific pathogen free (SPF) pigs.

In pilot study group number six a six-hour broth culture was prepared from the organism recovered in experiment number five and administered to a pig on days one, three, and five at a dosage of 100 ml. at each administration. Temperatures were again recorded twice a day for the duration of the acute signs.

Twelve specific pathogen free (SPF) pigs were purchased from

*Armo-vac - A, Armour Pharmaceutical Company, Kankakee, Illinois.

an SPF laboratory* to be used in the final part of this study. The four pigs in SPF group I, weighing approximately 30 pounds, were purchased on March 29 and placed in isolation facilities which had been thoroughly cleaned with pine oil disinfectant. Since these pigs had been fed an antibiotic in the feed, six days were allowed to elapse before administration of the organism was begun. Rectal temperatures were recorded twice a day beginning two days before administration of the culture and continuing until the pigs were all necropsied. Hemograms were performed two days prior to infection and continued every other day until completion of this group. The packed cell volume was determined by the microhematocrit method. The hemoglobin determination was performed by the cyanmethemoglobin method** using an automatic pipette delivering .02 ml. of blood and 6 ml. of reagent. The results were determined by reading the per cent transmission in a spectrophotometer and converting to gm./100 ml. by comparing with a chart prepared by determining the per cent transmission of known samples. Sahlm[26] reported the cyanmethemoglobin method as more accurate than some of the other methods which are sometimes used. The total white blood cell determination was performed by using an automatic pipette which delivered .02 ml. of blood and 10 ml. of saline giving a 1-500 dilution. The red blood cells were lysed by the addition of 0.11 ml. of a triton saponin solution. The sample was then placed in a Coulter Counter, model A,§ and the number of white blood cells were determined in 0.5 ml. of the

*Northwest Missouri SPF laboratory, Mound City, Missouri.
**Hycel, Inc., Box 36329, Houston 36, Texas.
§Coulter Electronics, Hialeah, Florida.

sample. Three such counts were made and the average taken. The final white blood cell number was computed by subtracting the background count of the saline from the average and then adding the correction factor prepared by Coulter Electronics[7] to allow for the possibility of more than one particle passing through the aperature at the same time. The Coulter Counter was set at a threshold of 15 and an A.P.C. of 4. The estimation of the cell type distribution was performed by making a thin smear of the thoroughly mixed sample and staining for eight minutes, after six minutes of fixation, with Wright's-Leishman Stain.[26] The slide was placed under oil immersion on a microscope and the cell types of 100 white blood cells was determined. All blood samples were drawn from the anterior vena cava in approximately eight ml. amounts using three or four drops of 10% dipotassium ethylenediamine tetracetate as an antocoagulant. Sterile needles and syringes were used to draw the sample.

On the day of infection one pig (number 1) was placed in one corner of the room behind a 30-inch solid panel to serve as a control. The other three pigs were drenched with a six-hour broth culture, each receiving 75 ml. Following this 100 ml. of the same broth culture was mixed with the feed both night and morning until the pigs quit eating. All four pigs received the same feed which was an equal mixture of ground corn, ground milo, and shorts. On necropsy, tissue samples of all organs were preserved in 10% buffered formalin for histopathological examination. It was necessary to euthanatize pigs number 1, 3, and 4 and this was achieved by intracardial injection of sodium pentabarbitol and

exsanguination by severing the brachial artery. Tissue samples of the liver, spleen, kidney, mesenteric lymph nodes, and ileum were taken for bacteriological examination as described previously. The formalized tissue was microsectioned and stained with hematoxylin-eosin for microscopic examination.

The eight SPF pigs in group II were purchased May 3. Pigs 5 through 8 weighed approximately 80 pounds and 9 through 12 weighed approximately 50 pounds. The same method was employed in recording temperatures and performing hemograms as was outlined in group I. Three of these pigs were segregated in another isolation room to serve as controls (6, 9, and 12). Pigs 5, 7, 8, 10, and 11 were given the broth culture of the same organism as in SPF group I. The culture was administered as a drench on the first day of infection in a 75 ml. per pig dose. From then on 200 ml. were added to the feed every night and morning. When a pig became anorectic it was again drenched with 50 ml. of the broth culture. Euthanasia, necropsies, and tissue collection and preservation were performed as previously described for group I.

Pigs 6 and 12 were given 100 ml. of the broth culture on May 21. On May 27 they were vaccinated with 2 ml. of a modified live lapinized hog cholera vaccine* without antiserum. On May 29 a broth culture of Salmonella choleraesuis var. kunzendorf was again administered and continued for four days at a level of 100 ml. per pig each day. Microsections of tissues from all these pigs were stained and studied for lesions.

*Armovac - A, Armour Pharmaceutical Company, Kankakee, Illnois.

RESULTS AND DISCUSSION

Pilot Studies

The attempts to produce salmonellosis in the commercial swine were mainly designed to determine the pathogenicity of the organism being used. In all cases there was a remarkable rise in temperature, up to 107-108 F. that indicated a septicemic condition had developed. In pilot studies two and four a diarrhea developed which indicated that besides a septicemia there was intestinal disturbance. One pig in pilot study number four was euthanatized six days after infection but no gross lesions could be found on necropsy; and on culturing the organism was not recovered. The other pig in pilot study four developed a diarrhea four days after inoculation and died eight weeks later with a chronic diarrhea. Post mortem decomposition was too well advanced for definite identification of lesions. The temperature elevation in all of these pigs occurred from 48-72 hours after introduction of the organism. At this same time the pigs became anorectic and lethargic. The temperature usually remained elevated for 24-36 hours and then returned to normal and the pigs resumed eating. During this febrile stage the pigs hair became roughened and the pigs lay in a corner of the pen. In pilot study five when the pig was vaccinated against hog cholera with modified live virus without serum and then given a Salmonella culture the syndrome observed was somewhat different. The febrile reaction was not as severe and diarrhea was not observed until the terminal stages. The hair became roughened and the pig became incoor-

dinated and unable to stand about 24 hours prior to death. On necropsy there was mild ulceration in the cecum and one small ulcer on the ileocecal valve. Salmonella choleraesuis var. kunzendorf was recovered from the liver, spleen, kidney, and mesenteric lymph nodes when cultured. These findings indicated that the condition had become septicemic and well disseminated in this pig.

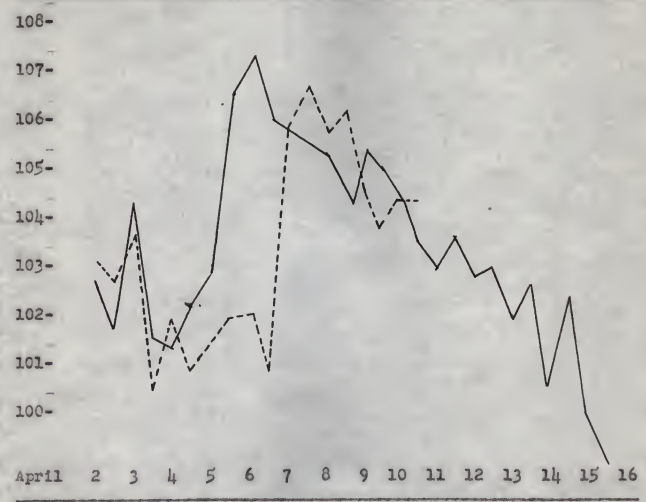
When the organism recovered from the above case was placed in another pig the febrile response was again observed but acute death did not occur.

SPF Studies -- Group I

The mean temperature response recorded for the pigs in group I is illustrated in table 1. The temperatures began rising about 36 hours after the introduction of the culture and reached the peak 12-24 hours later. The highest temperatures recorded for the three infected pigs in this group were from 107.8-108.1 F. At the time of initial febrile response the pigs became anorectic and lethargic. A profuse watery diarrhea was present in all of the infected pigs three days after infection and continued until all the pigs had either been euthanatized or died.

In studying the hemograms it was evident that a leukocytosis occurred and in the early stages of the infection a shift to the left was observed. The marked increase in white blood cells was particularly noticeable 48 hours after infection (Tables 2 and 3). Ninety-six hours after infection the white blood cell numbers had dropped to below the preinfection level indicating that as a result

Table 1. Mean bidaily temperature results in group I.



of a massive response due to the infection the bone marrow had apparently become depleted of cells. This is further substaniated by the large number of myelocytes, juveniles, and band cells that were present in the circulating blood and by the conspicuous absence of mature neutrophiles.

Pig 4 was euthanatized on the fourth day post inoculation with hopes of observing acute pathological lesions. The pathologic changes observed were mild compared to the lesions described

Table 2. Mean total leukocyte count in group I.

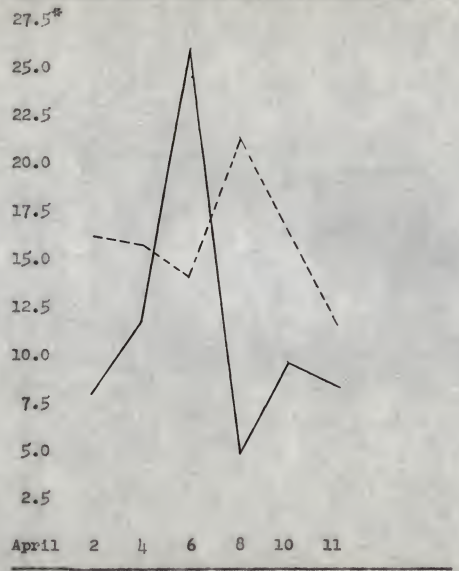
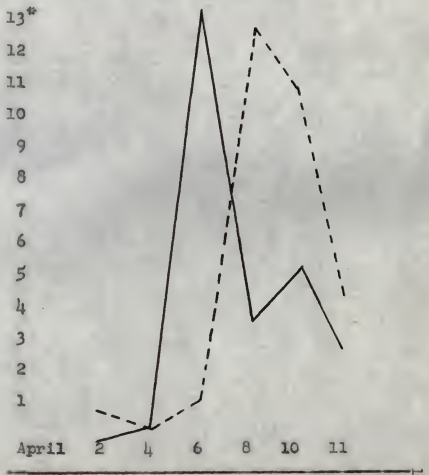


Table 3. Mean total immature cell group I.



* Count in thousands. _____Infected pigs .....Control pig

by Biester.[2] In the cardial portion of the stomach was a hemorrhagic area which was covered by a gray necrotic membrane. The mucosal surface of the ileum was hyperemic and slightly thickened but no errosions or areas of ulceration could be found. The mesenteric lymph nodes were swollen and edematous. There was a rather diffuse congestion of surface of the liver and kidneys. A few areas of congestion were observed in the lungs of this pig. S. choleraesuis was recovered from the mesenteric lymph nodes of this pig.

The remaining two pigs in this study regained a moderate appetite on the fifth post infection day and kept eating until 3 was euthanatized and 2 died.

Pig 3 was euthanatized on the seventh day post infection. At this time the pig was eating and the temperature was 103.5 F. On post mortem examination a few small hemorrhages were seen near the cardia in the stomach. The intestinal mucosa of the posterior jejunum, ileum, and centripetal colon was hyperemic. The mesenteric and gastric lymph nodes were enlarged, edematous, and slightly hemorrhagic. A slight diffuse congestion was seen on the liver which was rather friable. The spleen was much larger than normal and congested but since sodium pentabarbital was used for euthanasia the significance of this lesion could not be accurately determined. On bacteriological examination of tissues taken at necropsy S. choleraesuis was isolated and identified by the biochemical methods described earlier.

Pig 2 again quit eating on the eleventh day post infection and became lethargic and finally comatose before death on the thir-

teenth day after infection certain post mortem degenerative changes were observed since approximately six hours elapsed between the time of death and before a necropsy was performed. Examination of the stomach revealed areas of ecchymotic hemorrhages and small mucosal ulcers in the fundic portion. Petechial hemorrhages were seen on the mucosa in the posterior jejunum, ileum, cecum, and colon. The intestinal tract was empty but bile stained throughout with some blood in the posterior portion. The mesenteric and gastric lymph nodes were swollen and hemorrhagic. There were a few flecks of mucus mixed with the urine in the bladder and there were pockets of urine in the pelvis of the kidney. The adrenal glands appeared to be larger than normal. On bacteriological culture of the tissues S. choleraesuis was recovered from the liver, spleen, kidney, ileum, and mesenteric lymph nodes.

Pig 1 in this experiment was partitioned away from the other three but remained in the same room to serve as a control. Due to the fact that there was a febrile response and a white blood cell response and since S. choleraesuis var. kunzendorf was recovered from this pig on post mortem examination, it was concluded that this pig had become infected. Infection probably occurred from contaminated fecal material passing under the partition since drainage in this room was not as good as would have been desired. The rectal temperature of this pig began to rise 72 hours after the other pigs were infected and reached a peak 24 hours later. The total white blood cell count of this pig did not go as high as in the other cases but there was a shift to the left indicating response to an infection. This pig did not become anorectic and did not

develop the diarrhea that was seen in the other three pigs. This pig was euthanatized seven days following the initial infection of the other pigs. At this time the temperature of this pig was still slightly elevated. On post mortem examination there was some thickening of the intestinal mucosa with areas of shallow ulcer formation in the posterior jejunum and ileum. There was no congestion or hyperemia of these parts. The mesenteric and gastric lymph nodes were enlarged and edematous. A slight hyperemia was observed in the centripetal colon. The liver surface had a mottled appearance and the kidneys had a diffuse subcapsular hyperemia.

Histopathology of Pigs in Group I

Pig Number Four. The histologic lesions in this pig were mainly confined to the gastrointestinal tract and liver. The liver had proliferative nodules which were areas of degeneration of the liver cord cells with proliferation of lymphocytes, reticuloendothelial cells (R.E.) and a few neutrophils and eosinophils. The degeneration of the liver cord cells was evidenced by a more acidophilic reaction of cell cytoplasm and by karyorrhexis and pyknosis of the nucleus. These proliferative nodules were usually found in the peripheral one-half of the lobule often closely associated with the hepatic triad. The stomach had a mild inflammatory reaction with some infiltration of the lamina propria with lymphocytes and neutrophils. There were some detatched epithelial cells and bacterial colonies in the lumen. The small intestine was slightly hyperemic and a mild mucoid enteritis was present that became more severe in the ileum. The lamina propria of the jejunum was

infiltrated with a few lymphocytes, eosinophils, plasma cells, neutrophils, and R.E. cells. The lumen contained bacteria, some mucus, and partially digested plant and animal fibers. The same cellular reaction was present in the ileum but was more severe. There were a few areas of debridement of the surface epithelium in the ileum and the lymph nodules were enlarged and contained many R.E. cells. The crypts and glands were filled with necrotic debris which contained bacterial colonies especially in the area of the ileocecal valve. The mesenteric lymph nodes were enlarged and edematous with an increased number of neutrophils and R.E. cells and there appeared to be a lymphoid depletion. The colon had a mild inflammatory reaction with minimal cellular infiltration. The spleen was congested and the bronchi of the lung contained blood. This along with alveolar hemorrhage was probably the result of agonal aspiration resulting from a poor venipuncture at the time of euthanasia.

Pig Number Three. Proliferative nodules were observed in the liver of this pig and were much more distinct than those in pig 4. The cellular infiltration was more pronounced with lymphocytes and R.E. cells most evident and an occasional giant cell, neutrophil, and eosinophil observed. The degeneration of the liver cord cells was again obvious and the location of these nodules within the lobules was much the same as seen in pig 4. An inflammatory response was evident in the jejunum and ileum with cellular infiltration of the lamina propria essentially the same as that seen in pig 4. There was debridement of the surface epithelium and the lymph nodules were hyperplastic with an increase in R.E. cells, in some

of which mitotic figures were observed. The mesenteric lymph nodes were edematous and hypertrophic. There appeared to be an increase in the number of R.E. cells and neutrophils in the germinal centers of these nodes. The ileocecal valve was infiltrated with cells similar to those found in the ileum but necrotic material was not present in the mucosal glands. The colon had a mild inflammatory reaction with slight infiltration of the lamina propria. The spleen was congested and there was a slight increase in lymphocytes around the submeningeal vessels in the cerebrum.

Pig Number One. The proliferative nodules in the liver were again observed and cell types and arrangement were similar to that seen in the liver of pig 3. In this pig the nodules appeared to be closely associated with the hepatic triad in many instances. R.E. cells were somewhat more common in these nodules than in the previous two pigs. There was a mild inflammatory response in the jejunum and ileum which consisted of a slight increase in eosinophils in the lamina propria. Some of the mucus glands at the ileocecal valve were distended with necrotic material and the area was surrounded by a zone of lymphocytic infiltration and by a band of proliferating fibroblasts. The lymph follicles around the valve were enlarged and infiltrated with neutrophils and R.E. cells and the mucosa was infiltrated with inflammatory cells similar to those seen in pig 3. The mesenteric lymph nodes had an increased number of R.E. cells and neutrophils but not as severe as in pigs 3 and 4.

Pig Number Two. Post mortem autolysis was well advanced in the tissues of this pig. The proliferative changes found in the liver were mostly confined to the hepatic triad, quite often being

closely associated with the portal vein. There was slight infiltration of these areas with lymphocytes and neutrophils but the most marked change was the degeneration of the surrounding cord cells. The intestinal tract in this pig had marked post mortem autolysis but there was evidence indicating an inflammatory process had been present. In the jejunum and ileum inflammation of the lamina propria and lymph nodules was quite evident and the cellular changes present were essentially the same as those observed in the other pigs in this group. The ileocecal valve contained cysts of necrotic debris and bacteria which were surrounded by an inflammatory reaction with attempted walling off of the area. The increased size of the submucosal lymph nodules and mild infiltration of the lamina propria showed the inflammatory reaction extended into the colon in this pig.

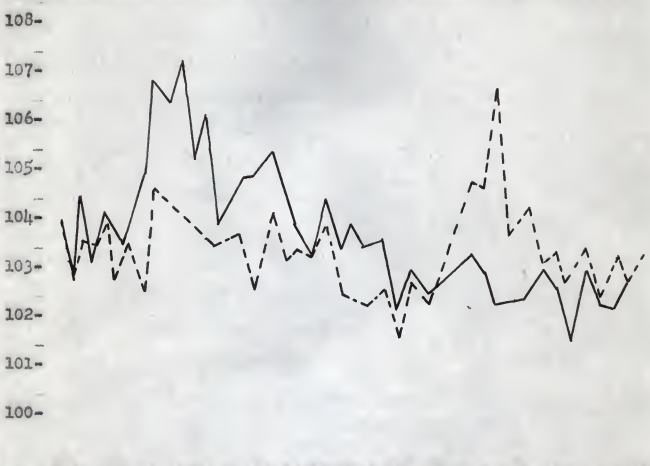
SPF Studies -- Group II

SPF group II contained eight pigs, four of which weighed about 80 pounds and were of mixed breeding. The other four were Duroc Jersey and weighed about 50 pounds. The larger pigs were numbered 5 through 8 and the smaller pigs were numbered 9 through 12.

Three of these pigs were moved to another isolation room to serve as controls. This group included one large pig and two smaller pigs.

The mean temperature of the infected pigs started to rise 36 hours after infection, reached a peak 48 hours after infection, and remained above normal for 96 hours after reaching the peak.

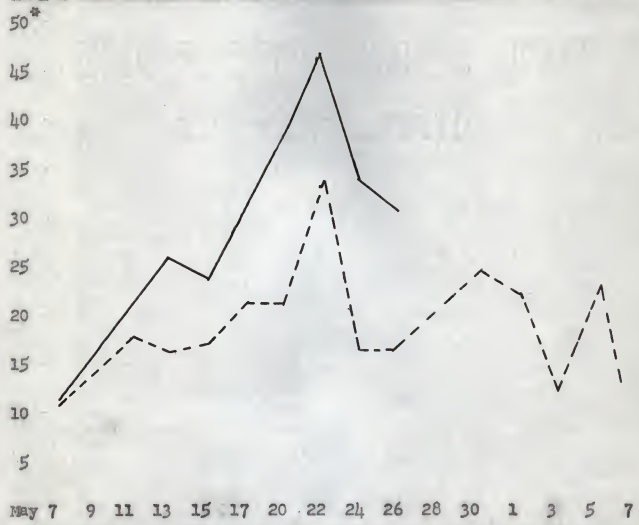
Table 4. Mean bidaily temperature results in group II.



———Infected pigs
.....Control pigs

This reaction is charted on table 4. The mean temperatures of the control pen remained within normal range during this time except on one occasion when the temperatures of two of the control pigs were slightly elevated. On May 21 when two of the control pigs were administered the broth culture the mean temperature rose to well above normal 48 hours later but the febrile state did not persist as long as it did in the pigs that were first infected. On May 27 the two pigs in the control group were vaccinated against

Table 5. Mean total leukocyte count in group II.

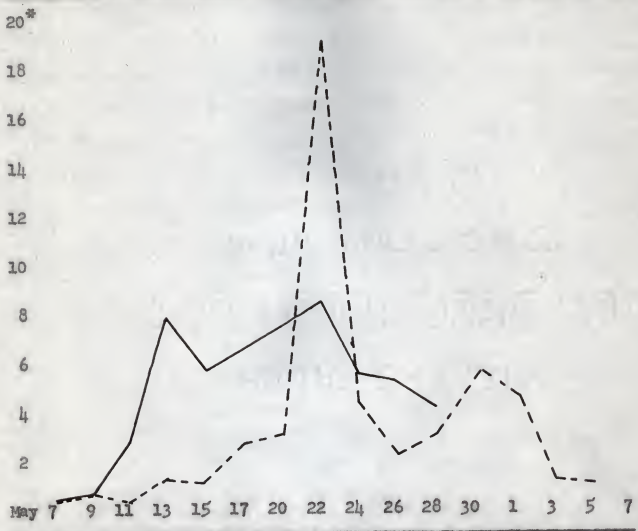


*In thousands ——— Infected pigs ····· Control pigs

hog cholera without using antiserum and again given the Salmonella choleraesuis var. kunzendorf culture. This time no noticeable temperature change occurred.

From blood studies on this group of pigs a marked leukocytosis was observed (Table 5). The total white blood cells gradually increased in number during the time the organism was being administered and started to decline only after the administration of the

Table 6. Mean total immature cell group II.



*In thousands ———Infected pigs ·····Control pigs

broth culture ceased. The absolute number of immature cells closely followed this trend indicating the bone marrow was stimulated and had responded to the infection (Table 6).

The control group, on the other hand, had a slightly increasing white blood cell level through the time of infection in the other pigs. When the controls were infected on May 21 they, too, had a rapid rise in leukocytes, but did not maintain the high level

for the duration of the organism administration as did the pigs in the infected group. The control pigs also had marked shift to the left 24 hours after infection but within 24 hours the absolute number of immature cells had dropped to near the preinfection level.

The clinical signs of infection were not as prevalent in this study as were those in the first study with SPF swine. Anorexia did develop in these pigs when infected but was very transitory lasting for only one or two feedings. This usually occurred when the peak febrile response was obtained. Diarrhea developed in pig 11 and was present at the time of euthanasia. In pig 10 diarrhea was evident for a period of 24 hours. In the other pigs in this study a diarrhea was never observed.

On May 14, five days after infection, pig 11 was euthanatized and necropsied. At this time the pig had a normal temperature and appetite. The lesions observed were not conclusive consisting of a slight reddening of the intestinal mucosa which grew more severe in the colon. There was diffuse congestion on the subcapsular surface of the kidney and a few areas of congestion in the apical lobes of the lungs. The mesenteric lymph nodes were enlarged and edematous and the mesenteric vessels were filled with blood. When the body was first opened the large intestine was distended with gas. S. choleraesuis was recovered from the mesenteric lymph nodes.

Pig 10 was euthanatized on May 18 and a necropsy performed. At this time the temperature of this pig had been within normal limits for a period of three days and the general appearance was normal. Upon post mortem examination the entire digestive tract was full of feed material of normal appearance. There was slight

congestion of the intestinal mucosa in the posterior jejunum and ileum becoming more severe in the colon. The right kidney had what appeared grossly to be an anemic infart in the cortex. The spleen was enlarged and dark but the significance of this lesion was hard to determine. There were a few areas of congestion in the lungs, primarily in the apical lobes. Bacteriological culturing produced S. choleraesuis from the mesenteric lymph nodes.

Pig 9 which had served as a noninfected control was necropsied at the same time as was pig 10. The digestive tract was full of feed and the spleen was enlarged and darkened. There was slight reddening of the mucosa in the centrifugal colon and few areas of congestion in the lungs. Bacteriological studies performed on the major organs of this pig were negative for Salmonella.

Euthanasia and a necropsy were performed on pig 8 on May 21. The temperature of this pig had remained within normal limits for a period of three days. This pig had not developed a diarrhea during the study and the only indication of illness was a brief period of lethargy. The only lesions noted were a mild hyperemia of the posterior jejunum, ileum, cecum, and colon and enlarged edematous mesenteric lymph glands. The spleen was enlarged and darkened. S. choleraesuis was recovered from the mesenteric lymph nodes.

On May 28 pigs 5 and 7 were euthanatized. There had been no elevation in the temperatures of these pigs for a period of eleven days and the general appearance of both was excellent. Upon post mortem examination of the pig 5 few lesions were found. There was a slight congestion of the surface of the liver and some

mild congestion of the intestinal mucosa. The congestion of the intestinal mucosa was probably hypostatic in nature since this pig had died before exsanguination was completed. The spleen was enlarged and there was a small area of congestion in the tip of the diaphragmatic lobe of the lung.

Pig 7 had a slight congestion on the surface of the liver. The gastrointestinal tract was grossly free of lesions. Bacteriological studies on both pig 5 and pig 7 were negative for Salmonella.

Pig 6 was one of the control group that received a culture of S. choleraesuis on May 21 and had been vaccinated against hog cholera on May 27 with the subsequent reintroduction of S. choleraesuis. On June 7 this pig was euthanatized and a necropsy was performed. At this time the temperature of this pig had remained within normal limits for 13 days and the general appearance was good. The only necropsy lesion observed in this pig was diffuse congestion of the subserous surface of the liver giving it a very mottled appearance. Attempts to isolate Salmonella from this pig were unsuccessful.

Pig 12 was a member of the control group and had received the same treatment as pig 6. This pig was euthanatized and a necropsy was performed on June 7. There had been no abnormal febrile reaction for 13 days prior to euthanasia. Post mortem examination revealed an intussusception with approximately two and one half inches of the ileum in the cecum. The serous surfaces of the intussuscepted ileum were well adhered indicating that this had been present for a period of time before death.

The lumen of the ileum within this lesion was approximately one-half inch in diameter and the flow of intestinal contents had not been seriously obstructed since there was minimal dilation of the ileum anterior to the lesion. Whether or not this lesion was present prior to infection or was a result of infection could not be determined. This lesion probably was not the result of infection since this pig did not have a diarrhea associated with the infection.

There were areas of congestion scattered throughout the lungs of this animal, and on the tip of the right diaphragmatic lobe there was a large thick-walled protuberance. This protuberance was approximately three inches in diameter and was beneath the pleura but was not in the lung tissue proper. When incised this lesion contained air and had a yellow-green exudate on the surface next to the lung tissue. A gram-negative lactose fermenting rod and a streptococci were cultured from this exudate. There were no adhesions between this lesion and the parietal pleura. The subserous surface of the liver and the subcapsular surface of the kidney were mottled with diffuse congestion. Salmonella was not isolated.

Histopathology of Pigs in Group II

Pig Number Eleven. The proliferative nodules observed in the liver of this pig were often closely associated with the hepatic triad and consisted of areas of cord cell degeneration with lymphocytes, R.E. cells, and some neutrophils present. The nuclei of the cord cells were pyknotic and karyorrhexic and often margination of the chromatin material was observed. The duodenum

had a mild inflammatory reaction in the lamina propria with an increase in lymphocytes, plasma cells, eosinophils, and R.E. cells. The inflammatory response was more severe in the jejunum with a more marked cellular infiltration and hyperemia of the mucosa. There appeared to be a particular increase in the number of eosinophils present in the lamina propria. There was evidence of slight distention of the submucosa with edema. The ileum was hyperemic and the lamina propria was infiltrated with cells similar to those seen in the jejunum. The surface epithelium was intact and pyknotic nuclear remnants were observed in the mucosa, submucosa, and lymph follicles. The lymph follicles were devoid of lymphocytes and R.E. cell hyperplasia was noted. Some of the glandular crypts in the region of the ileocecal valve were distended with necrotic debris. The colon was hyperemic and some inflammatory infiltration was present in the lamina propria and submucosa. The mesenteric lymph nodes were edematous and a few focal areas of necrosis were present. R.E. cell hyperplasia and lymphocyte depletion were noted in the germinal centers and increased neutrophils were seen in these lymph nodes. The spleen of this pig was congested and in one isolated area of the lung there was an acute supperative bronchial pneumonia.

Pig Number Ten. Proliferative nodules were observed in the liver of this pig but they were not as numerous as those seen in pig 11. Most of the inflammatory reaction was observed in the region of the hepatic triad with cellular infiltration similar to that in pig 11. There was a slight infiltration of the lamina propria of the duodenum with eosinophils, neutrophils, and R.E.

cells. The jejunum was hyperemic and had a mild cellular infiltration in the lamina propria. The lamina propria of the ileum had mild cellular infiltration and the lymph nodules had evidence of R.E. cell hyperplasia and edema. The mucosa of the ileum at the ileocecal valve had a moderate amount of cellular infiltration and the lymph nodules in this area were enlarged and pyknotic nuclear remains were observed throughout these nodules. The spleen and lungs were congested and evidence of emphysema and atelectasis was present in the lung tissue.

Pig Number Nine. A few nodules were seen in the liver of this pig but they were not as large or as numerous as in the other pigs. Lymphocytes and blast cells were the only cells observed in these nodules and the degeneration and necrosis of the liver cord cells seen in the other pigs was not seen in this case. The lamina propria of the intestines contained many eosinophils and a few other inflammatory cells. The lymph follicles of the ileum were enlarged but the R.E. cell hyperplasia was not as pronounced as in other cases. Mild atelectasis and emphysema were present in the lung.

Pig Number Eight. A few proliferative nodules were observed in the liver of this pig. These nodules were quite similar to the nodules observed in the other pigs studied. The cells that were present in these nodules consisted mainly of lymphocytes and R.E. cells with an occasional neutrophil and eosinophil. Degeneration and necrosis of the liver cord cells were present. A slight increase in inflammatory cells was present in the lamina propria of the duodenum. The lumen of the jejunum was filled with

partially digested plant and animal fibers and cellular debris. This part of the intestine was hyperemic with an infiltration of the lamina propria with more eosinophils than seen in other cases. In the ileum the mucosal glands were distended with mucus and in the lamina propria increased numbers of inflammatory cells were observed. R.E. cell hyperplasia was present in the lymph follicles along with an increased number of neutrophils and pyknotic nuclei. Some debridement of the surface epithelium and increased inflammatory reaction in the lamina propria was present in the mucosa of the ileocecal valve. The lungs were atelectatic and emphysemic and the spleen was congested.

Pig Number Five. A few proliferative nodules were observed in the liver of this pig but were not as numerous nor as large as those seen in other pigs. R.E. cell proliferation was most evident but lymphocytes and neutrophils were also present in these nodules. A mild inflammation of the lamina propria with cells of similar types as those observed in the other pigs was present in the duodenum. A marked cellular R.E. infiltration of the lamina propria and hyperemia was seen in the jejunum. The goblet cells of this portion of the intestine were numerous and filled with mucus. The lymph follicles of the ileum were hypertrophic, edematous, and R.E. cell hyperplasia was seen. Inflammation and excess mucus production was also seen in the ileum and became more severe near the ileocecal valve. Part of the lung had alveolar and bronchial hemorrhage along with atelectasis and emphysema.

Pig Number Seven. A few proliferative nodules were noted in the liver of this pig which were quite similar to those seen

in pig 5. The lumen of the duodenum and jejunum was filled with plant and animal material and there was a mild inflammation of the lamina propria. The lamina propria of the ileum had a marked increase in eosinophils and a moderate increase in the other inflammatory cells. The lymph nodules were enlarged, edematous, with a slight R.E. cell proliferation and the surface epithelium of the villi was missing in many places. There were a few areas of focal lymphocytic infiltration in the kidney and atelectasis and emphysema was present in the lung.

Pig Number Twelve. The proliferative nodules seen in the livers of the other pigs were not seen in this liver. There was a mild inflammation of the hepatic triad but not as severe as previously described. The duodenum and jejunum had a mild inflammatory reaction with some cellular infiltration of the lamina propria. More eosinophils were present in the mucosa of the jejunum and ileum than were seen in other parts of the intestine. The lymph follicles in the ileum were normal in size but evidence was present indicating a R.E. cell hyperplasia. The mucosa was completely missing from both surfaces of the part of the ileum which was intussuscepted into the cecum. Fibrous connective tissue was seen between the longitudinal muscle of these two parts indicating this lesion was of long duration. A mild inflammatory response was seen between the musculature bundles of the circular muscle and the submucosa was thickened and fibrous. Microscopic examination of the lesion described in the lung of this pig revealed a wall of fibrous connective tissue with little inflammatory response. On the inner surface of the cysts some crenated red

blood cells and fibrin deposits were found indicating this may have been a hematoma at one time with subsequent reabsorption of the contents, leaving a cyst filled with air. The lung tissue had some atelectatic and emphysemic areas.

Pig Number Six. Some proliferative nodules were present in the liver of this pig similar to those described for other pigs in this group. The inflammatory reaction in the intestinal tract was essentially the same as that found in the intestine of pig 12, except the lymph nodules were edematous and the goblet cells of the ileum were filled with mucus. A mild inflammatory response was present in the colon; and the lung had an area of atelectasis, hyperemia, and hemorrhage.

When the gross and microscopic changes present in the SPF pigs in groups I and II were compared with the lesions observed by other workers it was found that the lesions were similar except those observed in this study were not as severe as those described in literature by the other workers.

Whether or not the lesions described in the livers of these pigs are the same or similar to those described by Cohrs[6] as "Salmonella granulomas" could not be determined. More experimental work in this area will be required with particular emphasis on the histochemical reaction of these lesions and increased numbers of experimental animals to determine the frequency of occurrence of these lesions.

The lesions described in the intestinal tract of these pigs agreed very favorable but were not as severe as the lesions described by Murray[21] and by Biester.[2] The subcapsular hemorrhages

of the kidney described by Glasser[11] and often used as a diagnostic aid, were not observed in this study.

CONCLUSIONS

It was concluded that a culture of Salmonella choleraesuis var. kunzendorf administered to SPF pigs per os would cause a febrile response of a magnitude that is generally accepted as common in field cases of salmonellosis in swine.

An infection with Salmonella in the SPF pigs resulted in a leukocytosis and a shift to the left.

Experimental salmonellosis in SPF swine, produced by a pure culture of S. choleraesuis, did not result in lesions as severe as those described by other workers. It was therefore concluded that possibly some agent or agents or condition other than Salmonella may be responsible for the more severe lesions commonly observed.

A fatal septicemia or toxemia was produced by feeding a pure culture of S. choleraesuis var. kunzendorf.

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APPENDIX

Table 7. Bidaily temperatures recorded in group I.

Date	No. 1	No. 2	No. 3	No. 4
April 2 P.M.	103.0	102.6	102.4	103.0
April 3 A.M.	102.6	101.0	102.4	101.8
April 3 P.M.	103.4	104.0	104.2	104.0
April 4 A.M.	100.4	102.0	101.2	101.0
April 4 P.M.	101.8	101.4	101.0	101.3
April 5 A.M.	100.8	102.4	102.6	101.2
April 5 P.M.	101.4	103.0	102.9	102.5
April 6 A.M.	101.8	107.8	107.8	104.8
April 6 P.M.	101.9	106.5	107.4	108.1
April 7 A.M.	100.8	105.0	106.5	106.6
April 7 P.M.	105.7	105.2	105.0	107.2
April 8 A.M.	106.7	104.0	105.5	106.4
April 8 P.M.	105.6	104.6	105.9	---*
April 9 A.M.	106.2	103.8	104.9	---
April 9 P.M.	105.8	104.0	105.4	---
April 10 A.M.	103.8	104.0	106.0	---
April 10 P.M.	104.5	103.6	105.4	---
April 11 A.M.	104.3	103.6	103.5	---
April 11 P.M.	---*	104.4	---*	---
April 12 A.M.	---	103.0	---	---
April 12 P.M.	---	103.6	---	---
April 13 A.M.	---	102.8	---	---
April 13 P.M.	---	103.0	---	---
April 14 A.M.	---	102.0	---	---
April 14 P.M.	---	102.6	---	---
April 15 A.M.	---	100.6	---	---
April 15 P.M.	---	102.4	---	---
April 16 A.M.	---	100.0	---	---
April 16 P.M.	---	98.0	---	---
April 17 A.M.	---	---**	---	---

*Euthanatizia was performed.
**Natural death.

Table 8. Bidaily temperatures recorded in group II.

Date	No. 5	No. 6	No. 7	No. 8	No. 9	No.10	No.11	No.12
May 7 P.M.	102.9	104.0	104.3	103.6	103.8	104.0	103.9	104.0
May 8 A.M.	102.2	102.2	102.0	102.8	102.0	103.6	104.0	103.5
May 8 P.M.	105.7	103.2	104.0	103.4	103.2	103.6	105.2	104.1
May 9 A.M.	102.8	103.4	102.6	103.2	102.6	103.0	103.2	103.4
May 9 P.M.	103.2	104.4	104.4	105.2	104.4	102.8	104.8	103.6
May 10 A.M.	103.8	104.0	104.0	103.4	102.8	103.2	104.2	102.8
May 10 P.M.	102.2	104.4	103.8	103.6	102.3	102.5	104.9	103.3
May 11 A.M.	103.3	102.4	102.6	104.6	103.3	108.0	106.0	102.9
May 11 P.M.	106.2	104.0	105.6	106.4	103.6	107.6	106.9	104.0
May 12 P.M.	106.0	104.0	107.6	107.6	103.8	106.4	107.7	104.0
May 13 A.M.	105.2	102.8	106.2	104.9	104.0	104.4	105.8	104.4
May 13 P.M.	106.6	103.6	106.4	106.6	103.8	104.8	105.4	103.2
May 14 A.M.	102.2	104.4	106.0	104.4	103.4	103.8	103.0	103.1
May 14 P.M.	104.6	104.0	104.4	105.2	103.5	105.0	---*	103.2
May 15 A.M.	104.2	104.8	106.2	105.3	101.6	103.6	---	101.2
May 15 P.M.	104.4	106.0	105.0	106.6	103.4	104.6	---	103.0
May 16 A.M.	105.0	104.8	103.6	105.0	102.6	103.9	---	101.8
May 16 P.M.	102.6	104.6	102.4	105.8	103.0	103.8	---	102.4
May 17 A.M.	103.2	104.4	102.2	104.2	102.8	103.6	---	102.2
May 17 P.M.	104.8	105.4	104.2	105.0	103.0	103.6	---	103.0
May 18 A.M.	103.2	103.2	103.0	104.0	102.6	102.4	---	102.5
May 18 P.M.	104.0	105.4	103.0	104.4	---*	---*	---	101.8
May 19 A.M.	103.8	102.0	102.8	103.4	---	---	---	102.4
May 19 P.M.	103.0	102.4	102.8	104.3	---	---	---	102.6
May 20 A.M.	102.0	101.2	102.2	102.2	---	---	---	101.6
May 20 P.M.	103.2	102.6	102.0	103.4	---	---	---	102.6
May 21 A.M.	101.6	102.4	102.0	103.6	---	---	---	102.0
May 21 P.M.	102.4	102.2	103.0	---*	---	---	---	102.8
May 22 A.M.	103.4	102.2	102.6	---	---	---	---	105.4
May 22 P.M.	103.0	107.0	103.4	---	---	---	---	102.4
May 23 A.M.	103.0	104.3	102.6	---	---	---	---	104.8
May 23 P.M.	103.0	107.2	101.4	---	---	---	---	105.8
May 24 A.M.	102.4	104.2	102.0	---	---	---	---	102.6
May 24 P.M.	103.0	104.0	101.6	---	---	---	---	104.4
May 25 A.M.	103.4	102.8	102.4	---	---	---	---	103.2
May 25 P.M.	103.0	103.0	102.0	---	---	---	---	103.5
May 26 A.M.	101.4	102.4	101.8	---	---	---	---	102.8
May 26 P.M.	103.2	103.6	102.4	---	---	---	---	103.0
May 27 A.M.	102.5	102.6	101.8	---	---	---	---	101.8
May 27 P.M.	102.6	102.5	101.6	---	---	---	---	103.2
May 28 A.M.	103.0	102.6	102.4	---	---	---	---	102.6
May 28 P.M.	---*	103.2	---*	---	---	---	---	103.0
May 29 A.M.	---	102.6	---	---	---	---	---	102.8
May 29 P.M.	---	102.6	---	---	---	---	---	103.0
May 30 A.M.	---	102.5	---	---	---	---	---	103.4

(continued)

Table 8. (cont.)

Date	No. 5	No. 6	No. 7	No. 8	No. 9	No.10	No.11	No.12
May 30 P.M.	---	102.8	---	---	---	---	---	103.0
May 31 A.M.	---	102.0	---	---	---	---	---	103.4
May 31 P.M.	---	102.6	---	---	---	---	---	103.8
June 1 A.M.	---	102.4	---	---	---	---	---	103.0
June 1 P.M.	---	102.2	---	---	---	---	---	103.2
June 2 A.M.	---	101.6	---	---	---	---	---	103.8
June 2 P.M.	---	102.6	---	---	---	---	---	103.8
June 3 A.M.	---	101.5	---	---	---	---	---	102.7
June 3 P.M.	---	103.0	---	---	---	---	---	102.6
June 4 A.M.	---	102.2	---	---	---	---	---	101.0
June 4 P.M.	---	102.6	---	---	---	---	---	102.2
June 5 A.M.	---	102.0	---	---	---	---	---	101.6
June 5 P.M.	---	102.6	---	---	---	---	---	103.4
June 6 A.M.	---	102.5	---	---	---	---	---	102.5
June 6 P.M.	---	102.4	---	---	---	---	---	103.0
June 7 A.M.	---	102.5	---	---	---	---	---	102.2
June 7 P.M.	---	---*	---	---	---	---	---	---*

*Euthanatizia was performed.

Table 9a. Hemogram results on pig no. one in group I.

Date	W.B.C.*	Hb.	P.C.V.	Bas.	Eos.	Myelo.	Meta.	Band	Neut.	Lymph.	Mono.
April 2	16263	9.4	30%	---	3%	---	---	6%	12%	78%	1%
	---	---	---	---	487	---	---	975	1951	12685	162
April 4	15866	10.4	32%	1%	2%	---	---	2%	26%	68%	1%
	---	---	---	158	317	---	---	317	4125	10788	158
April 6	14480	10.4	36%	---	2%	---	3%	6%	23%	66%	1%
	---	---	---	---	289	---	434	868	3330	9556	144
April 8	21418	9.0	34%	---	1%	3%	11%	44%	36%	5%	---
	---	---	---	---	214	642	2355	9423	7710	1070	---
April 10	16648	9.6	32%	---	1%	---	10%	54%	10%	24%	1%
	---	---	---	---	166	---	1664	8989	1664	2995	166
April 11	11788	9.4	33%	---	2%	---	---	36%	23%	35%	3%
	---	---	---	---	235	---	---	4243	2711	4125	353

*Corrected for nucleated red blood cells.

Table 9b. Hemogram results on pig no. two in group I.

Date	W.B.C.*	Hb.	P.C.V.	Bas.	Eos.	Myelo.	Meta.	Band	Neut.	Lymph.	Mono.
April 2	5246	9.9	34%	---	4%	---	---	3%	49%	42%	2%
	---	---	---	---	209	---	---	157	2570	2203	104
April 4	10488	10.8	34%	---	2%	---	---	1%	29%	68%	---
	---	---	---	---	209	---	---	104	3041	7131	---
April 6	21169	8.6	28%	---	---	2%	11%	47%	31%	9%	---
	---	---	---	---	---	423	2328	9949	6562	1905	---
April 8	3490	8.8	33%	---	1%	9%	40%	16%	---	34%	---
	---	---	---	---	34	314	1396	558	---	1159	---
April 10	11395	11.4	37%	---	---	2%	7%	44%	3%	43%	1%
	---	---	---	---	---	227	797	5013	341	4899	113

*Corrected for nucleated red blood cells.

Table 9c. Hemogram results on pig no. three in group I.

Date	W.B.C.*	Hb.	P.C.V.	Bas.	Eos.	Myelo.	Meta.	Band	Neut.	Lymph.	Mono.
April 2	6754	9.6	33%	---	2%	---	---	1%	34%	57%	6%
	---	---	---	---	135	---	---	67	2296	3849	405
April 4	15064	10.2	33%	1%	2%	---	1%	1%	21%	70%	4%
	---	---	---	150	301	---	150	150	3163	10544	602
April 6	26783	9.4	31%	---	---	---	11%	48%	24%	17%	---
	---	---	---	---	---	---	2946	12855	6427	4553	---
April 8	4725	8.6	32%	---	---	1%	12%	42%	1%	42%	2%
	---	---	---	---	---	47	567	1984	47	1984	94
April 10	8042	9.8	32%	---	---	1%	1%	49%	2%	44%	3%
	---	---	---	---	---	80	80	3940	160	3538	241
April 11	8519	9.2	33%	---	---	---	3%	29%	12%	55%	3%
	---	---	---	---	---	---	255	2470	1022	4685	255

*Corrected for nucleated red blood cells.

Table 9d. Hemogram results on pig no. four in group I.

Date	W.B.C.*	Hb.	P.C.V.	Bas.	Eos.	Myelo.	Meta.	Band	Neut.	Lymph.	Mono.
April 2	12647	10.3	35%	---	1%	---	---	---	28%	64%	2%
	---	---	---	---	126	---	---	---	3541	8094	252
April 4	10468	10.0	34%	---	3%	---	2%	3%	46%	45%	2%
	---	---	---	---	314	---	209	314	4815	4710	209
April 6	30041	9.8	30%	---	---	---	3%	32%	42%	22%	1%
	---	---	---	---	---	---	901	9613	12617	6609	300
April 8	6835	7.8	25%	---	---	2%	21%	58%	---	19%	---
	---	---	---	---	---	136	1435	3964	---	1298	---

*Corrected for nucleated red blood cells.

Table 10a. Hemogram results on pig no. five in group II.

Date	W.B.C.	Hb.	P.C.V.	Bas.	Eos.	Myelo.	Meta.	Band	Neut.	Lymph.	Mono.
May 7	15005	13.5	39%	1%	2%	---	---	---	10%	86%	1%
	---	---	---	150	300	---	---	---	1500	12904	150
May 9	22679	12.3	40%	---	2%	---	---	3%	19%	76%	1%
	---	---	---	---	453	---	---	680	4309	17236	226
May 11	Clotted										
May 13	31950	11.6	38%	---	2%	---	---	32%	26%	37%	4%
	---	---	---	---	639	---	---	9904	8307	11821	1278
May 15	25846	9.6	32.5%	---	1%	---	1%	16%	24%	58%	---
	---	---	---	---	258	---	258	4135	6203	14990	---
May 17	34048	11.4	34%	---	1%	---	1%	15%	24%	57%	2%
	---	---	---	---	340	---	340	5107	8171	19407	680
May 20	42235	9.8	36%	1%	3%	---	---	16%	22%	58%	---
	---	---	---	422	1267	---	---	6757	9191	24496	---
May 22	42490	11.4	36%	---	1%	---	---	25%	27%	46%	---
	---	---	---	---	424	---	---	10622	11472	19545	---
May 24	49101	10.2	36%	---	2%	---	---	11%	37%	49%	1%
	---	---	---	---	982	---	---	5401	18167	24059	491
May 26	39106	10.4	35%	1%	1%	---	---	20%	37%	40%	1%
	---	---	---	391	391	---	---	7821	14469	15642	391
May 28	36631	10.7	34%	---	3%	---	---	18%	33%	43%	3%
	---	---	---	---	1098	---	---	6593	12088	15751	1098

Table 10b. Hemogram results on pig no. six in group II.

Date	W.B.C.	Hb.	P.C.V.	Bas.	Eos.	Myelo.	Meta.	Band	Neut.	Lymph.	Mono.
May 7	15822	12.7	40%	---	---	---	---	2%	19%	79%	1%
	---	---	---	---	---	---	---	316	3006	12499	158
May 9	26650	12.6	39%	---	2%	---	---	3%	29%	65%	1%
	---	---	---	---	533	---	---	799	7728	17322	266
May 11	17490	11.6	36%	---	1%	---	---	---	7%	92%	---
	---	---	---	---	174	---	---	---	1224	16090	---
May 13	19823	11.4	34%	---	1%	---	---	3%	33%	58%	5%
	---	---	---	---	198	---	---	594	6544	11503	991
May 15	26236	12.4	32%	---	1%	---	---	5%	36%	57%	1%
	---	---	---	---	262	---	---	1311	9444	14954	262
May 17	29235	11.6	33%	---	---	---	1%	16%	22%	58%	3%
	---	---	---	---	---	---	292	4677	6421	16956	877
May 20	26102	9.8	35%	---	3%	---	---	11%	18%	63%	5%
	---	---	---	---	783	---	---	2871	4698	16444	1305
May 22	30376	11.0	35%	---	3%	---	---	38%	16%	42%	1%
	---	---	---	---	911	---	---	11542	4860	12757	303
May 24	24006	10.8	34%	---	8%	---	1%	22%	---	65%	4%
	---	---	---	---	1920	---	240	5281	---	15603	960
May 26	22135	9.8	33%	---	4%	---	---	8%	11%	74%	3%
	---	---	---	---	885	---	---	1770	2434	16379	664
May 28	25923	10.8	33%	2%	3%	---	---	5%	22%	64%	4%
	---	---	---	518	777	---	---	1296	5703	16590	1036
May 30	25734	10.2	34%	---	5%	---	---	9%	14%	72%	---
	---	---	---	---	1286	---	---	2316	3602	18528	---
June 1	30665	10.2	31%	---	2%	---	---	20%	27%	49%	2%
	---	---	---	---	613	---	---	6133	8279	15025	613
June 3	13878	9.6	31%	1%	1%	---	---	---	10%	87%	1%
	---	---	---	138	138	---	---	---	1387	12073	138
June 5	22360	9.7	33%	---	3%	---	---	10%	16%	64%	7%
	---	---	---	---	447	---	---	2236	3577	14310	1565
June 7	15324	9.8	33%	---	2%	---	---	---	36%	57%	5%
	---	---	---	---	306	---	---	---	5516	8734	766

Table 10c. Hemogram results on pig no. seven in group II.

Date	W.B.C.	Hb.	P.C.V.	Bas.	Eos.	Myelo.	Meta.	Band	Neut.	Lymph.	Mono.
May 7	10122	13.5	41%	1%	5%	---	---	---	17%	77%	---
	---	---	---	101	506	---	---	---	1720	7793	---
May 9	16016	12.2	40%	---	5%	---	---	1%	25%	66%	3%
	---	---	---	---	800	---	---	160	4004	10570	480
May 11	15599	12.3	37%	2%	---	---	---	3%	23%	72%	---
	---	---	---	311	---	---	---	467	3587	11231	---
May 13	24111	12.3	34%	---	---	---	---	35%	38%	26%	1%
	---	---	---	---	---	---	---	8438	9162	6268	241
May 15	25236	10.2	32%	---	2%	---	---	38%	29%	31%	---
	---	---	---	---	504	---	---	9588	7317	7823	---
May 17	27438	10.8	33.5%	1%	5%	---	---	10%	25%	55%	1%
	---	---	---	274	1371	---	---	2743	6859	15090	274
May 20	35422	12.0	40%	1%	3%	---	1%	18%	27%	46%	4%
	---	---	---	354	1062	---	354	6375	9563	16294	1416
May 22	35211	12.3	37%	---	2%	---	---	17%	39%	41%	1%
	---	---	---	---	704	---	---	5985	13732	14436	352
May 24	43897	11.8	38%	2%	3%	---	---	13%	37%	44%	1%
	---	---	---	877	1316	---	---	5706	16241	19314	438
May 26	29141	11.6	37%	---	9%	---	---	10%	32%	47%	2%
	---	---	---	---	2622	---	---	2914	9325	13696	582
May 28	24398	11.2	37%	---	6%	---	---	7%	23%	61%	3%
	---	---	---	---	1463	---	---	1707	5611	14882	731

Table 10d. Hemogram results on pig no. eight in group II.

Date	W.B.C.	Hb.	P.C.V.	Bas.	Eos.	Myelo.	Meta.	Band	Neut.	Lymph.	Mono.
May 7	15822	12.2	39.5%	1%	2%	---	---	---	14%	79%	4%
	---	---	---	158	316	---	---	---	2215	12499	632
May 9	17764	12.6	40%	1%	---	---	---	2%	22%	73%	---
	---	---	---	177	---	---	---	355	3908	12967	---
May 11	26819	12.6	41%	---	1%	---	---	1%	41%	57%	---
	---	---	---	---	268	---	---	268	10995	15286	---
May 13	33734	11.6	37%	---	4%	---	---	14%	25%	56%	1%
	---	---	---	---	1349	---	---	4722	8433	18891	337
May 15	27467	10.8	38%	---	1%	---	4%	15%	36%	42%	2%
	---	---	---	---	274	---	1098	4120	9888	11536	549
May 17	34903	11.8	38%	---	3%	---	1%	24%	26%	45%	---
	---	---	---	---	1047	---	349	8376	9074	15706	---
May 20	36748	10.2	34%	---	---	---	---	23%	7%	68%	2%
	---	---	---	---	---	---	---	8452	2572	24988	734

Table 10e. Hemogram results on pig no. nine in group II.

Date	W.B.C.	Hb.	P.C.V.	Bas.	Eos.	Myelo.	Meta.	Band	Neut.	Lymph.	Mono.
May 7	9331	12.0	38%	---	5%	---	---	2%	49%	42%	2%
	---	---	---	---	446	---	---	186	4572	3919	186
May 9	9487	12.3	39%	---	1%	---	---	5%	48%	46%	---
	---	---	---	---	94	---	---	474	4553	4364	---
May 11	Clotted										
May 13	19054	10.9	34%	---	2%	---	---	16%	48%	35%	---
	---	---	---	---	381	---	---	3048	9145	6668	---
May 15	14450	10.8	32%	---	4%	---	2%	5%	45%	44%	---
	---	---	---	---	578	---	289	722	6502	6358	---
May 17	18279	11.4	38%	1%	8%	1%	---	14%	33%	43%	---
	---	---	---	182	1462	182	---	2559	6032	7859	---

Table 10f. Hemogram results on pig no. ten in group II.

Date	W.B.C.	Hb.	P.C.V.	Bas.	Eos.	Myelo.	Meta.	Band	Neut.	Lymph.	Mono.
May 7	5959	11.8	39%	---	2%	---	---	2%	42%	54%	---
	---	---	---	---	119	---	---	119	2502	3217	---
May 9	12334	13.0	40%	1%	---	---	---	1%	50%	47%	1%
	---	---	---	123	---	---	---	123	6166	5796	123
May 11	27226	12.0	39%	---	---	---	---	24%	50%	26%	---
	---	---	---	---	---	---	---	6534	13613	7078	---
May 13	10935	11.4	36%	---	2%	---	---	33%	17%	46%	2%
	---	---	---	---	218	---	---	3608	1858	5030	218
May 15	14748	10.0	34%	---	1%	---	1%	22%	29%	47%	---
	---	---	---	---	147	---	147	3244	4276	6931	---
May 17	24768	11.2	36.5%	---	5%	1%	6%	29%	28%	29%	1%
	---	---	---	---	1238	247	1486	7182	6935	7182	247

Table 10g. Hemogram results on pig no. eleven in group II.

Date	W.B.C.	Hb.	P.C.V.	Bas.	Eos.	Myelo.	Meta.	Band	Neut.	Lymph.	Mono.
May 7	7515	11.4	34%	---	---	1%	---	3%	45%	51%	1%
	---	---	---	---	---	75	---	225	3381	3832	75
May 9	10107	11.6	38%	---	1%	---	---	3%	32%	61%	3%
	---	---	---	---	101	---	---	303	3234	6165	303
May 11	14994	11.6	33%	---	---	---	---	22%	57%	21%	---
	---	---	---	---	---	---	---	3298	8546	3148	---
May 13	27497	10.4	32%	---	---	---	1%	46%	27%	26%	---
	---	---	---	---	---	---	274	12648	7424	7149	---

Table 10h. Hemogram results on pig no. twelve in group II.

Date	W.B.C.	Hb.	P.C.V.	Bas.	Eos.	Myelo.	Meta.	Band	Neut.	Lymph.	Mono.
May 7	5973	12.7	38%	1%	---	---	---	---	22%	75%	2%
	---	---	---	59	---	---	---	---	1314	4479	119
May 9	7404	11.8	36.5%	---	1%	---	---	1%	14%	83%	1%
	---	---	---	---	74	---	---	74	1036	6145	74
May 11	Clotted										
May 13	10058	12.0	38%	---	---	---	---	12%	44%	41%	3%
	---	---	---	---	---	---	---	1206	4425	4123	301
May 15	11489	10.4	34%	---	3%	---	---	12%	37%	47%	---
	---	---	---	---	344	---	---	1378	4250	5399	---
May 17	16297	12.0	37.5%	---	---	---	2%	12%	20%	62%	2%
	---	---	---	---	---	---	325	1955	3259	10104	325
May 20	16769	10.4	38%	---	2%	---	---	19%	23%	56%	---
	---	---	---	---	335	---	---	3186	3856	9390	---
May 22	36811	10.2	32%	---	---	---	---	71%	17%	12%	---
	---	---	---	---	---	---	---	26135	6257	4417	---
May 24	9104	12.4	31.5%	1%	7%	---	3%	37%	---	48%	4%
	---	---	---	-91	637	---	273	3368	---	4369	364
May 26	10613	9.0	29%	---	7%	---	1%	20%	9%	62%	1%
	---	---	---	---	742	---	106	2122	955	6580	106
May 28	14646	14.8	33%	---	6%	---	---	35%	16%	43%	2%
	---	---	---	---	878	---	---	5126	2343	6297	292
May 30	22118	10.4	36%	---	1%	---	---	41%	26%	30%	---
	---	---	---	---	221	---	---	9068	5750	6635	---
June 1	13258	9.4	32%	---	---	---	1%	25%	31%	42%	1%
	---	---	---	---	---	---	132	3314	4109	5568	132
June 3	9591	9.6	31%	---	---	---	---	28%	34%	38%	---
	---	---	---	---	---	---	---	2685	3260	3644	---
June 5	Clotted										
June 7	9363	9.6	32%	1%	---	---	---	2%	36%	56%	5%
	---	---	---	93	---	---	---	187	3370	5243	468

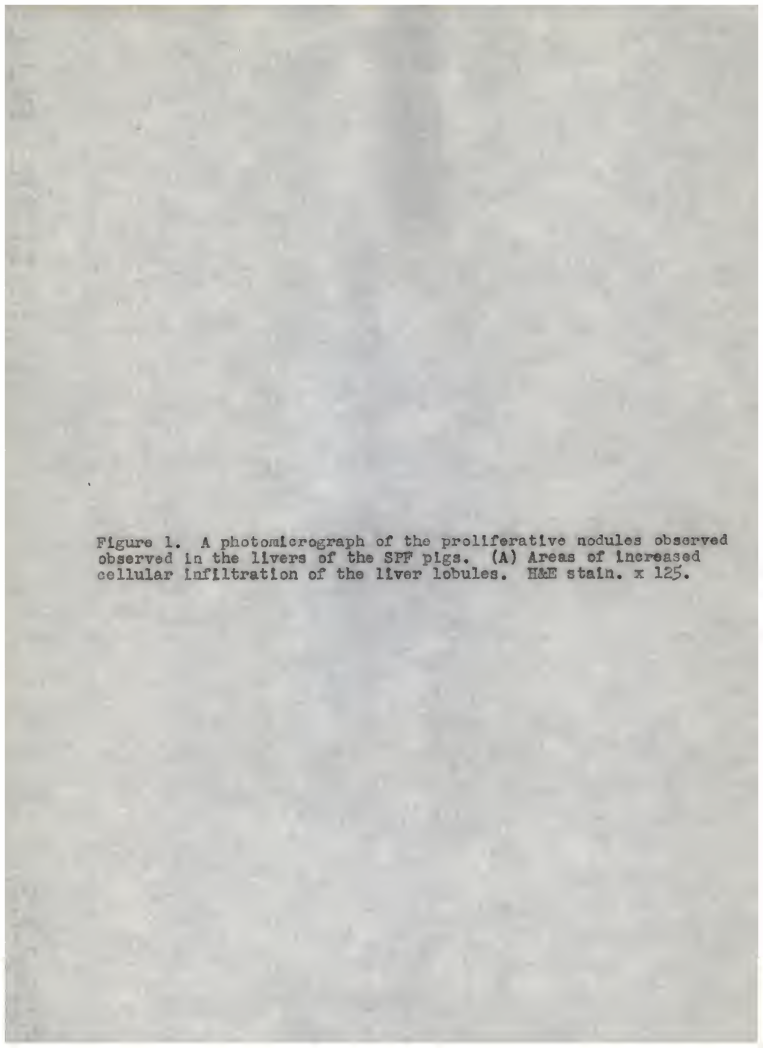


Figure 1. A photomicrograph of the proliferative nodules observed observed in the livers of the SPF pigs. (A) Areas of increased cellular infiltration of the liver lobules. H&E stain. x 125.

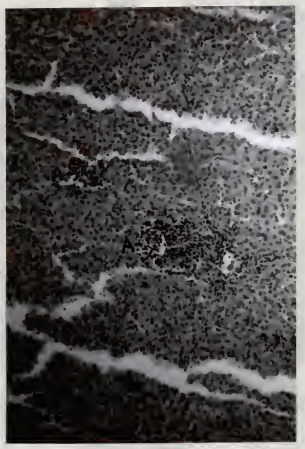


Figure 2. A higher magnification of the same nodule as in figure 1. (A) R.E. cells. (B) Lymphocytes. (C) Degenerating liver cord cells. H&E stain. x 500.

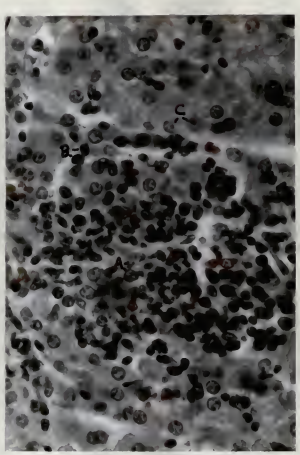

C
B

Figure 3. A higher magnification of a proliferative nodule in the liver of a SPF pig showing more cellular degeneration than was seen in figure 2. (A) R. E. cells. (B) Lymphocytes. (C) Degenerate liver cord cells. H&E stain. x 500

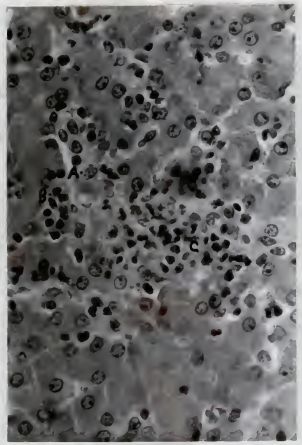
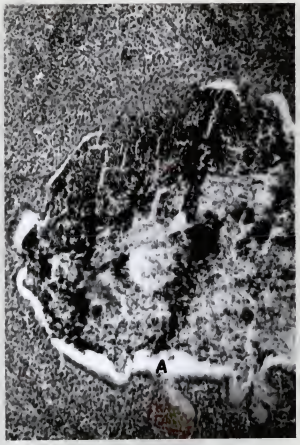

A

Figure 4. A photomicrograph of the mucosa of the ileum showing cellular infiltration of the lamina propria. (A) Germinal center of a lymph follicle. H&E stain. x 125.

Figure 5. A higher magnification of the lamina propria of the ileum. (A) R.E. cells. (B) Lymphocytes. (C) Eosinophil. H&E stain. x 500.


B
A
C

Figure 6. A photomicrograph showing the necrotic debris in a mucosal gland near the ileocecal valve. (A) Glandular epithelium. H&E stain. x 125.


A

PATHOLOGY OF EXPERIMENTAL ACUTE SALMONELLOSIS IN SPECIFIC PATHOGEN FREE SWINE

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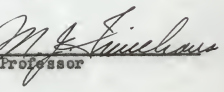

Major Professor

ABSTRACT

The study on acute salmonellosis in specific pathogen free (SPF) swine was designed to determine the pathology associated with this condition. The organism used was Salmonella choleraesuis var. kunzendorf which had been isolated from a case of salmonellosis in a pig at Kansas State University. Ten commercial pigs were used in pilot studies to determine the pathogenicity of this organism before administration to the SPF pigs. The twelve SPF pigs used were obtained from a certified SPF laboratory and were kept in isolation quarters from the time of purchase until the completion of the experiments. The organism was administered per os either by drenching or by mixing it with the feed as a 6-14 hour broth culture. The administration of the organism was continued for periods of from 4 to 11 days and was given both morning and evening at a dosage of 50-75 ml. per pig.

The rectal temperatures of these pigs became elevated to 107-108 F. approximately 48 hours after infection and returned to normal approximately 96 hours later. The leukocytosis present in all the infected pigs reached a peak from 24 to 48 hours after infection and then the total leukocyte count either returned to normal as in group I or continued to rise, as in group II, for the duration of the time the culture was administered. A shift to the left was observed. The maximum numbers of immature cells reached a peak at the same time as the maximum leukocyte response was observed.

A diarrhea appeared in five of the eleven pigs that were either infected or became infected. One animal died as a result

of the infection and the other ten were euthanatized. The necropsy lesions were not as severe as those reported by other workers in experimentally produced salmonellosis. A mild reddening of the intestinal mucosa with a few petechial hemorrhages in the ileum were seen in the pigs which had a diarrhea. Microscopically proliferative nodules were observed in the livers of most of the infected pigs. These lesions were characterized by the presence of degenerative liver cord cells, an increased number of neutrophils, eosinophils, lymphocytes, and reticulo endothelial (R.E.) cells. The proliferative nodules were often closely associated with the hepatic triad but also were observed in the peripherial one-half of the lobule. The jejunum and ileum had an inflammatory response with hyperemia and increased numbers of lymphocytes, eosinophils, neutrophils, and R.E. cells present in the lamina propria. The lymph nodules of these parts of the intestine were hyperplastic and hypertrophic. There were necrotic foci in the submucosa of the ileum at the ileocecal valve and the mesenteric lymph nodes were enlarged and edematous with R.E. cell hyperplasia.